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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: METHOD FOR THE HUMANIZATION OF ANTIBODIES AND HUMANIZED ANTIBODIES THEREBY OBTAINED

(57) Abstract: Method for the humanization of the VH and VL variable regions of an animal antibody of known sequence, humanized animal antibody obtainable according to the method, in particular anti-NGF and anti-TrkA humanized animal antibodies.

WO 2005/061540 A3

INTERNATIONAL SEARCH REPORT

Inter: International Application No

PC1/1T2004/000722

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07K16/00 C07K16/46 C07K16/28 C07K16/22 G06F19/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, Sequence Search

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>QUEEN C ET AL: "A HUMANIZED ANTIBODY THAT BINDS TO THE INTERLEUKIN 2 RECEPTOR" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, NATIONAL ACADEMY OF SCIENCE. WASHINGTON, US, vol. 86, no. 24, 1 December 1989 (1989-12-01), pages 10029-10033, XP000310534 ISSN: 0027-8424 page 10031, right-hand column, lines 11-17, 32-38, 41-44 figure 2</p> <p>----- -/--</p>	1-6



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
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- *8* document member of the same patent family

Date of the actual completion of the international search

3 August 2005

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INTERNATIONAL SEARCH REPORT

Inter. ¹ al Application No

PCT/IT2004/000722

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	RAMSLAND PAUL A ET AL: "Crystal structures of human antibodies: A detailed and unfinished tapestry of immunoglobulin gene products." JOURNAL OF MOLECULAR RECOGNITION, vol. 15, no. 5, 2002, pages 248-259, XP002338674 ISSN: 0952-3499 page 255, right-hand column, lines 47-58 page 256, left-hand column, lines 10-14 page 256, right-hand column, line 50 - page 257, left-hand column, line 4 -----	1-6
X	WO 02/096458 A (GENENTECH, INC; SHELTON, DAVID, L) 5 December 2002 (2002-12-05) example 1a page 9, lines 11-27 page 24, line 26 - page 15, line 8 -----	7,8
X	WO 00/73344 A (SIRS SOCIETA' ITALIANA PER LA RICERCA SCIENTIFICA; NOVAK, MICHAL, M; L) 7 December 2000 (2000-12-07) sequence 2 claims 2,3 -----	7,9
P,X	WO 2004/058184 A (RINAT NEUROSCIENCE CORP; SHELTON, DAVID, L; PONS, JAUME; ROSENTHAL, AR) 15 July 2004 (2004-07-15) example 1 -----	7,8
T	COVACEUSZACH SONIA ET AL: "Neutralization of NGF-TrkA receptor interaction by the novel antagonistic anti-TrkA monoclonal antibody MNAC13: a structural insight." PROTEINS. 15 FEB 2005, vol. 58, no. 3, 15 February 2005 (2005-02-15), pages 717-727, XP002338675 ISSN: 1097-0134 the whole document -----	1-9

INTERNATIONAL SEARCH REPORT

International application No.

PCT/IT2004/000722

Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.b of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, the international search was carried out on the basis of:
 - a. type of material
 - ☒ a sequence listing
 - ☒ table(s) related to the sequence listing
 - b. format of material
 - ☒ in written format
 - ☒ in computer readable form
 - c. time of filing/furnishing
 - ☐ contained in the international application as filed
 - ☐ filed together with the international application in computer readable form
 - ☒ furnished subsequently to this Authority for the purpose of search
2. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional comments:

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/IT2004/000722

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 02096458	A	05-12-2002	BR 0210231 A	14-09-2004
			CA 2448956 A1	05-12-2002
			EP 1401498 A1	31-03-2004
			JP 2004536072 T	02-12-2004
			MX PA03010911 A	17-02-2004
			NZ 529612 A	19-12-2003
			WO 02096458 A1	05-12-2002
			US 2004219144 A1	04-11-2004
			ZA 200308999 A	19-11-2004
WO 0073344	A	07-12-2000	IT RM990333 A1	27-11-2000
			AT 263188 T	15-04-2004
			AU 776457 B2	09-09-2004
			AU 5101900 A	18-12-2000
			CA 2373274 A1	07-12-2000
			DE 60009484 D1	06-05-2004
			DE 60009484 T2	24-03-2005
			DK 1181318 T3	12-07-2004
			EP 1181318 A2	27-02-2002
			ES 2218163 T3	16-11-2004
			WO 0073344 A2	07-12-2000
			JP 2003502029 T	21-01-2003
			PT 1181318 T	31-08-2004
WO 2004058184	A	15-07-2004	AU 2003299898 A1	22-07-2004
			WO 2004058184 A2	15-07-2004
			US 2004237124 A1	25-11-2004